Protein and Amino Acids

Proteins form the major structural components of all the cells of the body. Proteins also function as enzymes, in membranes, as transport carriers, and as hormones. Amino acids are constituents of protein and act as precursors for nucleic acids, hormones, vitamins, and other important molecules. Thus, an adequate supply of dietary protein is essential to maintain cellular integrity and function, and for health and reproduction.

The requirements for protein are based on careful analyses of available nitrogen balance studies. Data were insufficient to set a Tolerable Upper Intake Level (UL). DRI values are listed by life stage group in Table 1. The Acceptable Macronutrient Distribution Range (AMDR) for protein is 5–20 percent of total calories for children 1 through 3 years of age, 10–30 percent of total calories for children 4 to 18 years of age, and 10–35 percent of total calories for adults older than 18 years of age.

For amino acids, isotopic tracer methods and linear regression analysis were used whenever possible to determine requirements. The estimated average requirements (EARs) for amino acids were used to develop amino acid scoring patterns for various age groups based on the recommended intake of dietary protein. Data were insufficient to set a Tolerable Upper Intake Level (UL) for any of the amino acids. However, the absence of a UL means that caution is warranted in using any single amino acid at levels significantly above those normally found in food.

Proteins found in animal sources such as meat, poultry, fish, eggs, milk, cheese, and yogurt provide all nine indispensable amino acids and are referred to as "complete proteins." Proteins found in plants, legumes, grains, nuts, seeds, and vegetables tend to be deficient in one or more of the indispensable amino acids and are called "incomplete proteins."

Both protein and nonprotein energy (from carbohydrates and fats) must be available to prevent protein-energy malnutrition (PEM). Similarly, if amino acids are not present in the right balance, the body's ability to use protein will be affected. Protein deficiency has been shown to affect all organs and many systems. The risk of adverse effects from excess protein intake from food appears to be very low. The data are conflicting on the potential for high-protein diets to produce gastrointestinal effects, changes in nitrogen balance, or chronic disease, such as osteoporosis or renal stones.

PROTEIN AND THE BODY

Function

Protein is the major functional and structural component of every cell in the body. All enzymes, membrane carriers, blood transport molecules, the intracellular matrices, hair, fingernails, serum albumin, keratin, and collagen are proteins, as are many hormones and a large part of membranes. Amino acids are constituents of protein and act as precursors for many coenzymes, hormones, nucleic acids, and other important molecules.

The most important aspect and defining characteristic of protein from a nutritional point of view is its amino acid composition (amino [or imino] nitrogen group). Amino nitrogen accounts for approximately 16 percent of protein weight, and so nitrogen metabolism is often considered to be synonymous with protein metabolism. Amino acids are required for the synthesis of body protein and other important nitrogen-containing compounds as mentioned above. The amino acids that are incorporated into protein are α-amino acids, with the exception of proline, which is an α-imino acid.

Nutritional and Metabolic Classification of Amino Acids

Different sources of protein widely vary in chemical composition and nutritional value. Although amino acids have been traditionally classified as indispensable (essential) and dispensable (nonessential), accumulating evidence on the metabolic and nutritional characteristics of dispensable amino acids has blurred their definition, forming a third classification called conditionally indispensable. The term conditionally indispensable recognizes that under most normal conditions, the body can synthesize these amino acids.

The nine indispensable amino acids are those that cannot be synthesized to meet the body's needs, and therefore must be obtained from the diet. The five dispensable amino acids can be synthesized in the body. Six other amino acids are conditionally indispensable because their synthesis can be limited under special pathophysiological conditions, such as prematurity in the young infant or individuals in severe catabolic stress. Table 2 lists the classification of amino acids in the human diet.

Protein Quality

The quality of a source of dietary protein depends on its ability to provide the nitrogen and amino acid requirements that are necessary for the body's growth, maintenance, and repair. This ability is determined by two factors: digestibility and amino acid composition. Digestibility affects the number and type of amino acids made available to the body. If the content of a single indispensable

TABLE 2 Indispensable, Dispensable, and Conditionally Indispensable Amino Acids in the Human Diet

Indispensable	Dispensable	Conditionally Indispensable[a]	Precursors of Conditionally Indispensable
Histidine[b]	Alanine	Arginine	Glutamine/glutamate, aspartate
Isoleucine	Aspartic acid	Cysteine	Methionine, serine
Leucine	Asparagine	Glutamine	Glutamic acid/ammonia
Lysine	Glutamic acid	Glycine	Serine, choline
Methionine	Serine	Proline	Glutamate
Phenylalanine		Tyrosine	Phenylalanine
Threonine			
Tryptophan			
Valine			

[a] Conditionally indispensable is defined as requiring a dietary source when endogenous synthesis cannot meet metabolic need.

[b] Although histidine is considered indispensable, unlike the other eight indispensable amino acids, it does not fulfill the criteria of reducing protein deposition and inducing negative nitrogen balance promptly upon removal from the diet.

amino acid in the diet is less than the individual's requirement, then this deficiency will limit the utilization of other amino acids and thus prevent normal rates of protein synthesis, even when the total nitrogen intake level is adequate. As a result, the "limiting amino acid" will determine the nutritional value of the diet's total nitrogen or protein content.

The concept of the "limiting amino acid" has led to the practice of amino acid (or chemical) scoring, whereby the indispensable amino acid composition of a given protein source is compared with that of a reference amino acid composition profile to evaluate the quality of food proteins or their capacity to efficiently meet both nitrogen and indispensable amino acid requirements.

Absorption, Metabolism, Storage, and Excretion

Amino acids are present in the body as free amino acids or as part of protein. They are available through two major pathways: dietary intake in the form of proteins or de novo synthesis by the body.

When proteins are ingested from food, they are denatured by stomach acid. In the stomach, they are also cleaved into smaller peptides by the enzyme pepsin, which is activated in response to a meal. The proteins and peptides then enter the small intestine, where a variety of enzymes hydrolyze the peptide bonds. The resulting mix of free amino acids and peptides is transported into the mucosal cells. The amino acids are then either secreted into the blood or further metabolized within the cells. Absorbed amino acids pass into the liver, where some are taken up and used and others are circulated to and used by the peripheral tissues.

About 43 percent of the total protein content of the body is present as skeletal muscle, while other structural tissues, such as skin and blood, each contain approximately 15 percent of the body's total protein. The metabolically active visceral tissues (e.g., liver and kidney tissue) contain comparatively small amounts of protein (together about 10 percent of the total). Other organs such as the brain, heart, lung, and bone contribute the remainder. Almost half of the total protein content of the body is represented by only four proteins (myosin, actin, collagen, and hemoglobin).

Amino acids are lost in the body by oxidation, excretion, or conversion to other metabolites. Metabolic products of amino acids, such as urea, creatinine, and uric acid, are excreted in the urine; fecal nitrogen losses may account for 25 percent of the obligatory loss of nitrogen. Other routes of loss of intact amino acids are through the sweat and other body secretions and through the skin, nails, and loss of hair.

Protein Turnover

The process by which all body proteins are being continuously broken down and resynthesized is known as protein turnover. From a nutritional and metabolic point of view, it is important to recognize that protein synthesis is a continuing process that takes place within most of the body's cells. In a steady state, when neither net growth nor protein loss is occurring, protein synthesis is balanced by an equal amount of protein degradation.

The major consequence of inadequate protein intake, or of consuming diets that are low or lacking in specific indispensable amino acids, is a shift in this balance. Rates of synthesis of some body proteins decrease while protein degradation continues in order to provide an endogenous source of the amino acids most in need. The mechanism of intracellular protein degradation by which protein is hydrolyzed to free amino acids is more complex and not as well characterized at the mechanistic level as that of protein synthesis.

The daily amount of protein turned over is greater in infants and less in the elderly when compared with young adults on a body-weight basis; and some body tissues are more active than others with regard to it. Despite their rather small contribution to the total protein content of the body, the liver and the intestine together are believed to contribute as much as 50 percent of whole body protein turnover. Conversely, although skeletal muscle is the largest single component of body protein mass (43 percent), it contributes only about 25 percent to total body protein turnover.

DETERMINING DRIS

Determining Requirements

PROTEIN

The requirements for protein were based on careful analyses of available nitrogen balance studies.

AMINO ACIDS

Age-based recommendations were set for all nine of the indispensable amino acids found in dietary proteins (see Appendix E). These requirements are based on isotopic tracer methods and linear regression analysis, which were used whenever possible.

The requirements for amino acids and for total protein were used to develop a new FNB/IOM Protein Scoring Pattern for use in children aged 1 year and older and in all other age groups. The recommended amino acid scoring pattern for proteins for individuals aged 1 year and older and all other age groups is as follows (in mg/g of protein): isoleucine, 25; leucine, 55; lysine, 51; methionine + cysteine (SAA), 25; phenylalanine + tyrosine, 47; threonine, 27; tryptophan, 7; valine, 32; and histidine, 18. This pattern allows comparison of the relative nutritional quality of different protein sources by calculating a protein digestibility corrected amino acid score (PDCAAS). The calculation compares the amino acid in a test protein with the amount of that amino acid in the FNB/IOM scoring pattern multiplied by the true digestibility. Illustration of the calculation involved is detailed in *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids* (2005).

Special Considerations

Multiparous pregnancies: Multiparous pregnancies are associated with a marked increase in low birth weight and perinatal mortality. Thus, it is logical to assume that women supporting the growth of more than one fetus have higher protein needs, and some evidence supports this assumption. Thus, it is prudent that women carrying twins should increase their protein intake by an additional 50 g/day beginning in the second trimester, as well as ensure for themselves a sufficient energy intake to utilize the protein as efficiently as possible.

Physically active individuals: It is commonly believed that athletes should consume a higher-than-normal protein intake to maintain optimum physical performance. However, since compelling evidence of additional need is lacking, no additional dietary protein is suggested for healthy adults who undertake resistance or endurance exercise.

Vegetarian diets: Individuals who restrict their diet to plant-based foods may be at risk of deficiencies in certain indispensable amino acids because the concentration of lysine, sulfur amino acids, and threonine are sometimes lower in plant proteins than in animal proteins. However, vegetarian diets that include complementary mixtures of plant proteins can provide the same quality of protein as that from animal proteins. Available evidence does not support recommending a separate protein requirement for individuals who consume complementary mixtures of plant proteins.

Criteria for Determining Protein Requirements, by Life Stage Group

Life stage group	*Criterion*
0 through 6 mo	Average consumption of protein from human milk
6 through 12 mo	Nitrogen equilibrium plus protein deposition
1 through 18 y	Nitrogen equilibrium plus protein deposition
> 18y	Nitrogen equilibrium
Pregnancy	Age-specific requirement plus protein deposition
Lactation	Age-specific requirement plus milk nitrogen

The AMDR

The Acceptable Macronutrient Distribution Range (AMDR) for protein is 5–20 percent of total calories for children 1 through 3 years of age, 10–30 percent of total calories for children 4 to 18 years of age, and 10–35 percent of total calories for adults older than 18 years of age (see Part II, "Macronutrients, Healthful Diets, and Physical Activity").

The UL

The Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse effects for almost all people. Data were insufficient to establish a UL for total protein or for any of the amino acids. However, the absence of a UL warrants caution in using any single amino acid at levels significantly above those normally found in food.

PROTEIN SOURCES

Foods

Proteins from animal sources such as meat, poultry, fish, eggs, milk, cheese, and yogurt provide all nine indispensable amino acids and are referred to as "complete proteins." Proteins from plants, legumes, grains, nuts, seeds, and vegetables tend to be deficient in one or more of the indispensable amino acids and are called "incomplete proteins."

Dietary Supplements

With the exception of discussion of amino acids from all sources, this information was not provided at the time the DRI values for protein and amino acids were set. Given limited data, caution is warranted in using any single amino acid at a level significantly above that normally found in food.

Bioavailability

(See "Protein Quality.")

Dietary Interactions

This information was not provided at the time the DRI values for protein and amino acids were set.

INADEQUATE INTAKE AND DEFICIENCY

Both protein and nonprotein energy (from carbohydrates and fats) must be available to prevent protein-energy malnutrition (PEM). Similarly, if amino acids are not present in the right balance, the body's ability to use protein will be affected.

Worldwide, PEM is fairly common in both children and adults and is associated with the deaths of about 6 million children each year. In the industrialized world, PEM is predominately seen in hospitals, is associated with disease, or is often found in the elderly.

Protein deficiency has been shown to affect all of the body's organs and many of its systems, including the brain and brain function of infants and young children; the immune system, thus elevating risk of infection; gut mucosal function and permeability, which affects absorption and vulnerability to systemic disease; and kidney function.

The physical signs of protein deficiency include edema, failure to thrive in infants and children, poor musculature, dull skin, and thin and fragile hair. Biochemical changes reflecting protein deficiency include low serum albumin and low serum transferrin.

EXCESS INTAKE

Protein

The risk of adverse effects from excess protein intake from foods appears to be very low. The data are conflicting on the potential for high-protein diets to produce gastrointestinal effects, changes in nitrogen balance, or chronic disease, such as osteoporosis or renal stones. Further research is needed in these areas.

Amino Acids

There is no evidence that amino acids derived from usual or even high intakes of protein from food present any risk. Data were limited on the adverse effects of high levels of amino acid intakes from dietary supplements and therefore caution is warranted in using any single amino acid at a level significantly above that normally found in food.

Special Considerations

Maple syrup urine disease (MSUD): MSUD is the most common disorder associated with genetic anomalies in the metabolism of branched-chain amino acids (BCAAs), such as leucine, isoleucine, and valine. The condition stems from inadequate function of a multienzyme system called branched-chain ketoacid dehydrogenase and is characterized by elevated plasma levels of BCAAs, especially leucine. Although MSUD can be diagnosed in infancy, there are six other forms of the condition that begin later in life. People with MSUD must severely restrict their consumption of BCAAs. Without proper treatment and medical management, mental retardation and death may occur.

Phenylketonuria (PKU): PKU is a genetic disorder that impairs activity of the enzyme phenylalanine hydroxylase (PAH). This allows phenylalanine or by-products of its breakdown to build up in the plasma during critical periods of brain development. Chronically elevated plasma phenylalanine levels before and during infancy and childhood can cause irreversible brain damage, growth retardation, and skin abnormalities. To prevent these problems, dietary phenylalanine must be restricted within one month of birth and this restriction continued at least through childhood and adolescence. In the United States, approximately 1 of every 15,000 infants is born with PKU.

KEY POINTS FOR PROTEIN AND AMINO ACIDS

✓ Protein is the major functional and structural component of every cell in the body. All enzymes, membrane carriers, blood transport molecules, the intracellular matrices, hair, fingernails, serum albumin, keratin, and collagen are proteins, as are many hormones and a large part of membranes.

✓ The amino acids that make up proteins act as precursors for nucleic acids, hormones, vitamins, and other important molecules.

✓ The most important aspect and defining characteristic of protein from a nutritional point of view is its amino acid composition (amino [or imino] nitrogen group).

✓ Although amino acids have traditionally been classified as indispensable (essential) and dispensable (nonessential), accumulating evidence on the metabolic and nutritional characteristics of dispensable amino acids has blurred their definition, forming a third classification called conditionally indispensable.

✓ The quality of a source of dietary protein depends on its ability to provide the nitrogen and amino acid requirements that are necessary for the body's growth, maintenance, and repair.

✓ The adult requirements for protein are based primarily on nitrogen balance studies.

✓ The Acceptable Macronutrient Distribution Range (AMDR) for protein is 5–20 percent of total calories for children 1 through 3 years of age, 10–30 percent of total calories for children 4 to 18 years of age, and 10–35 percent of total calories for adults older than 18 years of age.

✓ Data were insufficient to establish a UL for total protein or amino acids.

✓ Proteins from animal sources such as meat, poultry, fish, eggs, milk, cheese, and yogurt provide all nine indispensable amino acids and are referred to as "complete proteins."

✓ Proteins from plants, legumes, grains, nuts, seeds, and vegetables tend to be deficient in one or more of the indispensable amino acids and are called "incomplete proteins."

✓ Both protein and nonprotein energy (from carbohydrates and fats) must be available to prevent protein-energy malnutrition (PEM).

- ✓ Protein deficiency has been shown to affect all of the body's organs and many systems.
- ✓ The data are conflicting on the potential for high-protein diets to produce gastrointestinal effects, changes in nitrogen balance, or chronic disease, such as osteoporosis or renal stones.
- ✓ There is no evidence that amino acids derived from usual or even high intakes of protein from food present any risk. Data were limited on the adverse effects of high levels of amino acid intakes from dietary supplements and therefore caution is warranted in using any single amino acid at a level significantly above that normally found in food.

TABLE 1 Dietary Reference Intakes for Water by Life Stage Group

	DRI values (L/day)[a]
	AI[b]
Life stage group[c]	
0 through 6 mo	0.7, assumed to be from human milk
7 through 12 mo	0.8 of *total*[d] water, assumed to be from human milk, complementary foods and beverages. This includes approximately 0.6 L (about 3 cups) as total fluid, including formula or human milk, juices, and drinking water.
1 through 3 y	1.3 of *total* water. This includes approximately 0.9 L (about 4 cups) as total beverages, including drinking water.
4 through 8 y	1.7 of *total* water. This includes approximately 1.2 L (about 5 cups) as total beverages, including drinking water.
9 through 13 y	
males	2.4 of *total* water. This includes approximately 1.8 L (about 8 cups) as total beverages, including drinking water.
females	2.1 of *total* water. This includes approximately 1.6 L (about 7 cups) as total beverages, including drinking water.
14 through 18 y	
males	3.3 of *total* water. This includes approximately 2.6 L (about 11 cups) as total beverages, including drinking water.
females	2.3 of *total* water. This includes approximately 1.8 L (about 8 cups) as total beverages, including drinking water.
19 through > 70y	
males	3.7 of *total* water. This includes approximately 3.0 L (about 13 cups) as total beverages, including drinking water.
females	2.7 of *total* water. This includes approximately 2.2 L (about 9 cups) as total beverages, including drinking water.

TABLE 1 Continued

	DRI values (L/day)[a]
	AI[b]
Pregnancy	
14 through 50 y	3.0 of *total* water. This includes approximately 2.3 L (about 10 cups) as total beverages, including drinking water.
Lactation	
14 through 50 y	3.8 of *total* water. This includes approximately 3.1 L (about 13 cups) as total beverages, including drinking water.

[a] Conversion factors: 1 L = 33.8 fluid oz; 1 L = 1.06 qt; 1 cup = 8 fluid oz.

[b] **AI** = Adequate Intake. If sufficient scientific evidence is not available to establish an Estimated Average Requirement (EAR), and thus calculate a Recommended Dietary Allowance (RDA), an AI is usually developed. For healthy breast-fed infants, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all healthy individuals in the group, but a lack of data or uncertainty in the data prevents being able to specify with confidence the percentage of individuals covered by this intake.

[c] Life stage groups through 8 years of age represent males and females.

[d] *Total* water (as italicized) includes all water contained in food, beverages, and drinking water. For infants, 7 through 12 months, *total* water assumed to be from human milk, complementary foods and beverages.